VERSION WITH MARKINGS TO SHOW CHANGES MADE

On page 82:

(3) The site-directed recombination enzyme is expressed in [a mouse ES cell] chicken DT-40 cells retaining the human chromosome (fragment) produced in (2) above. The promoter sequence and the GFP gene are joined together in the cell, wherein site-directed recombination occurs between the loxP sequences, so that the GFP is expressed. That is, chicken DT-40 cells comprising recombinant human chromosomes resulting from translocation can be selected.

On Page 281:

(2) Preparation of anti-TNF-α [human IgM antibody] human IgG antibody

The chimeric mouse CLH13-13 (derived from TT2FES clone LH13, 50% chimerism) as produced in Example 67-(3) was immunized with human TNF-α, thereby producing hybridomas. Human Tumor Necrosis Factor-α (TNF-α, PEPRO TECH EC LTD., 300-01A) dissolved in PBS was mixed with adjuvant (MPL + TDM Emulsion, RIBI Immunochem Research Inc.) to prepare 0.025 mg/ml TNF-α solution. 0.2ml of the TNF-α solution was used for immunization by 5 times intraperitoneal injection at 1 week interval. Two weeks after the fifth immunization, the TNF-α solution was used to boost the immunization. Two weeks after boosting, the chimeric mouse was immunized with 0.025 mg/ml TNF-α solution dissolved in PBS. The blood was collected every week, and the anti-TNF-α human Igγ concentration in serum was detected by ELISA according to Example 14. As shown in Fig. 50, an increased human Igγ antibody titer against TNF-α was shown. Three days after final immunization, the spleen was excised from the chimeric mouse, followed by cell fusion with PEG according to Example 24, thereby

producing hybridomas. The fused cells were diluted to achieve 250 thousand spleen cells / ml in a medium (Sanko Junyaku Co., Ltd. S-Clone Cloning Medium CM-B)

On Page 286:

(1) Analysis of single Tc/KO mice

First, the following four types of analysis (A) to (D) were performed for a total of 189 offspring produced by the mating above. A search was performed for a mouse (single Tc/KO), which meets only [two of the above conditions] conditions of retaining sc20 fragment and being homozygous for heavy chain deficiency (retaining no W23 fragment, and being heterozygous or wild type for κ chain-deficiency). In these individuals, B lymphocytes were developed by function of human heavy-chain introduced instead of mouse heavy-chain that had been deleted. In addition, most of the antibody molecules in sera were thought to contain human heavy-chain.

On Page 290:

(2) Analysis of double Tc mice

The following four types (A) to (D) of analysis were made for a total of 189 offspring born. A search was done for mouse mice (double Tc), which meet [at least [redacted] conditions] at least a condition of retaining sc20 fragment and W23 fragment and express human heavy-chain and human κ chain simultaneously.